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**COMMENTARY ON RECENT TRENDS OF COVID-19 TILL END OF MARCH 2020,
UPBRINGING AND SUGGESTED MANAGEMENT: A CRITICAL REVIEW AND
REPORT**

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ABSTRACT

COVID-19 is caused by Coronavirus related to SARS family is the major cause of morbidity and mortality across the world in current time specifically in USA, Europe and China. USA faced major effects and about 190000 persons has been affected till date and about 43000 deaths globally has been declared. Virus is related to negative sense RNA viruses. Two invading organisms have been isolated responsible for current outbreak. HCoV-NL63 is α coronaviruses while HCoV-HKU1 is from the class of β -coronaviruses. All countries are struggling hard to counter this pandemic disease, the percent population spread in the New York State of USA is 0.390 which is curiously high. The procedures adopted by China and South Korea to stand against pandemic are highly appreciable.

Keywords: COVID-19, SARS, Coronavirus, HCoV-NL63, HCoV-HKU1, Pandemic

1. INTRODUCTION

Corona viruses (CoVs) are belonged to largest assembly Nidovirales order, including Coronaviridae, Arteriviridae and Roniviridae families. The CoVs sectioned into four groups as alpha, beta, gamma, delta corona viruses [1] among those alpha and beta can infect mammals while later two may affect birds in addition to dose on mammals [2]. Virions of Coronavirus stand spherical [3, 4], in addition to this they have club shape prickly outcrop provide the appearance of solar corona, endorsing the name coronavirus. Coronaviruses take helically regular nucleocapsids, which is unusual among positive-sense RNA viruses and common for negativesense RNA viruses. They may contain four types of structural protein as spike (S), membrane (M), envelop (E) and nucleocapsid (N). All are encoded by 3' end of the genome [5, 6], the primary attachment of the virion to the host cell is started by communications between the S protein and its receptor [7]. Corona viruses were only considered to cause a self-limiting respiratory infection before the SARS-CoV outbreak. Two of these human corona viruses are α corona viruses (HCoV-229E and HCoV-NL63) whereas the further two are β -coronaviruses (HCoV-OC43 and HCoV-HKU1). HCoV-229E and HCoV-OC43 were

isolated almost 50 years back [8, 9, 10], but HCoV-NL63 and HCoV-HKU1 were lately recognized succeeding the SARS-CoV outbreak [11, 12], these are widespread in human causing 15-30% respiratory tract infection each year primarily attack on newborn, old and patients with underlying illness. As it may cause demyelinating disease so it is proposed that CoVs may involve in progress of multiple sclerosis (MS) [13].

2. BACKGROUND

Unusual Pneumonia by SARS-Cov recognized initially in Guangdong, China, then swiftly spread to Beijing, Hong Kong Vietnam Singapore and Canada in March 2003 [14, 15], in the 2002–2003 epidemic of China about 8098 cases arose with 774 expiries, resultant in a death rate of 9%. This proportion was ample higher in elderly individuals, with mortality rates approaching 50% in persons completed 60 years of age [16].

3. CURRENT SPREAD

In December 2019, Wuhan the metropolitan of China, again disclosed outbreak of an innovative coronavirus, which was named by WHO on January 7th 2020 as Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) and the

subsequent sickness caused by the virus known as corona virus disease 2019, (COVID-19) [17], by the end of March 2020 the total infected count was 872696 with 43269 death across the world [18].

3.1. Spread in European countries in comparison with China

The first case was seen on 10th Jan 2020 in China there while on February 20th 2020 the cases exceed to a count of 75000 registered cases with 2236 deaths. With the end of March the spike break and just 7544 more cases added from 20th Feb to 31st March 2020 reaching to about 81544 registered cases and addition of 1064 deaths, to a sum of total 3300 mortalities. The most advantageous outcome was cure of about 76238 patients with the best management in the world. On the other hand the 1st case in Italy and Spain was seen on 29th January and 30th January 2020 respectively. Despite of having best health care system both remain unable to control the pandemic and at the end of March 31st 2020 the total count of registered cases in Italy reach to a peak of 105792, outcome was achieved for only 28157 cases with 15729 (56%) cure and 12428 (44%) death. The major issue was pendency in cases of about 73612 cases showing the compromised situation of health care system of the Italy. Spain which was

smashed acutely after Italy crosswise the Europe also showed the compromised condition having 102136 registered cases, with 31700 closed cases including 22647, i.e. 71% recovery and 9053, i.e. 29% death. While about 70436 pending cases. We report the key difference between China and European countries was percent of cure in defined period of time which is reasonably extraordinary in China and drop in submission of fresh cases which was controlled in China by spreading general awareness about less spread of pandemic disease among community by means of strict administrative strategies. Like Italy and Spain other countries of Europe including Germany, France, Switzerland and Austria had received a stern hit from this epidemic disease till 31st March 2020 (18), as shown in (Figure 1).

3.2. Spread in US in comparison with China

The more intense position was witnessed in US, the first case was observed on 20th January 2020 and till 20th February 2020 there were only 15 cases, the count reached to 3613 till 15 the March 2020 but after that a zoomed increased was observed and the count was reached to 19567 in next five days i.e. on 20th March. It was rocketed increase to a level of 68211 in another 5 days and effects

become out of control at end of month when the count has crossed the 188592 level. The daily new cases in US from 15th march to 31st march is described in **(Figure 2)** and **(Table 1)**.

We report that China is the country with largest population in the world comprises of 1.437 Billion, and US has a count of about 330.5 million about 1/5th of the total population of China, the onset of disease in china was 10 days before US i.e. 10th of January 2020, the spread in China was below 82000 people in 80 days while its was above 188000 people in just 70 days, at the end of month the cases with no outcome in US were more than 177285 while in China the figure was below 2500 with a maximum cure of about 76238 person from 81544 infected ones, showing the best management of the nation as shown in **(Figure 3)**.

3.3. Spread across the Africa

COVID-19 hit 46 countries of Africa among 54 countries, with a death number of 146 and total cases were 4613 [19] **(Table 2)**. We find Lesotho, Comoros, Sierra Leone, South Sudan, Burundi, Botswana, Sao Tome and Principe, & Malaw were virus free countries till 31st March 2020.

3.4. Spread in Arabic countries in comparison with China

In Arab countries situation was much better as compare to China, US and Europe, the most affected country was KSA with cases about 1500, with 10 deaths and recovery of 13 patients, Qatar 693, UAE 611, Bahrain 516 and Kuwait 616.

3.5. Spread in Soth Asian Countries in comparison with Iran

Among Pakistan, Iran, Afghanistan, India, Srilanka and Bangladesh. Iran was hit harder than Pakistan, which stand 2nd before India. The first case reported in Iran was on 18th February and count augmented very harshly ranges to a level of about 47593 including 3036 deaths 16 %, while a very successful rate of recovery of about 84% (15473) among 18509 closed cases were observed. Pakistan was 2nd country among this region having 2042 cases including 26 casualties. India having 1590 cases with 45 deaths, Afghanistan has 196 cases with 4 deaths, Srilanka 143 with 2 deaths and Bangladesh having 54 cases with 6 deaths **(Figure 4)**.

The recovery percent is better in south Asian countries with the best result of Srilanka so far **(Figure 5)**, Pakistan and India were also in better situation as per rate of recovery despite of compromised economic, political and health conditions.

3.6. Spread across the US states

COVID-19 hit almost all states of USA, while the level of occurrence is significantly high in New York and New Jersey. Where 0.39 and 0.20% of the population is infected, which is higher than any other state of the any country of the world (Table 3, Figure 6).

Italy is among most smashed country of the Europe, has total population is about 60.46 million total infected persons were 105792, 0.17 percent of the population was affected, 0.21% population of Spain affected, while in New York it was 0.39%, which was quite alarming.

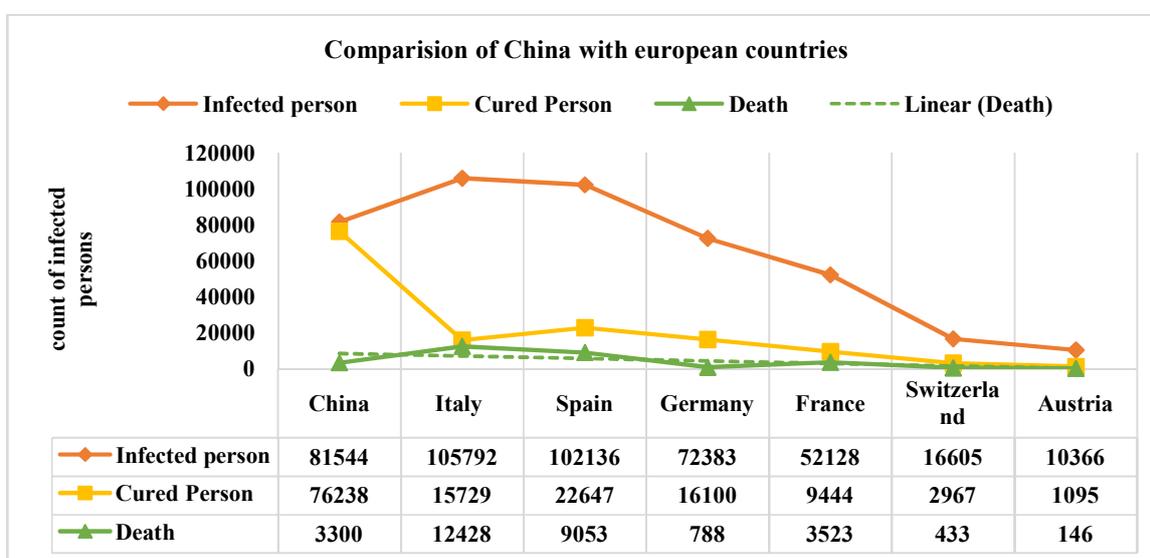


Figure 1: Comparison of China with european countries

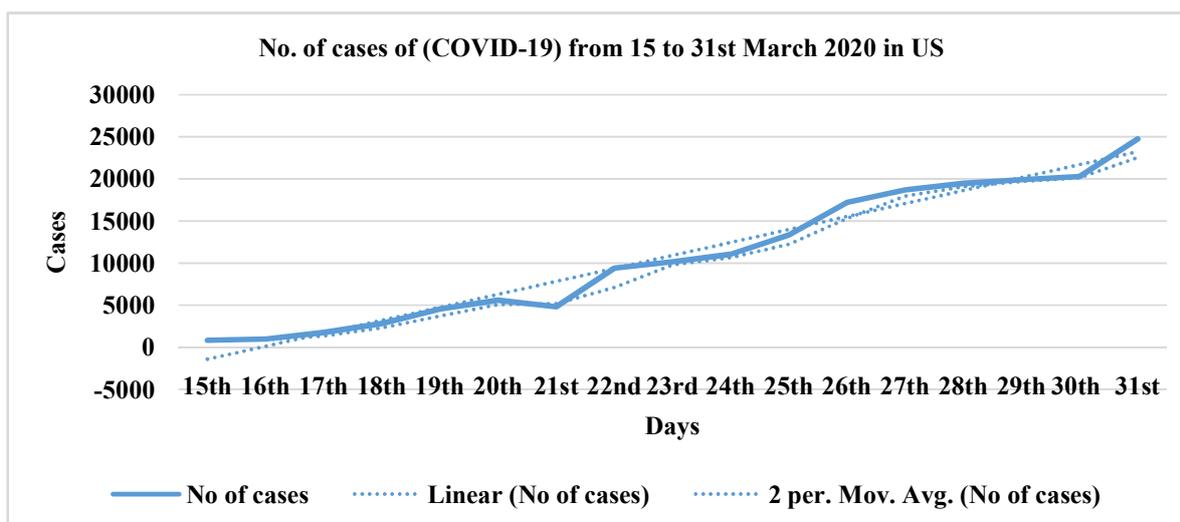


Figure 2: No. of cases of (COVID-19) from 15 to 31st March 2020 in US

Table 1: No. of cases of (COVID-19) from 15 to 31st March 2020 in US

S/No	Day of March	No of cases
1	15th	843
2	16th	983
3	17th	1748
4	18th	2853
5	19th	4582
6	20th	5588
7	21st	4825
8	22nd	9400
9	23rd	10189
10	24th	11075
11	25th	13355
12	26th	17224
13	27th	18691
14	28th	19452
15	29th	19913
16	30th	20297
17	31st	24742

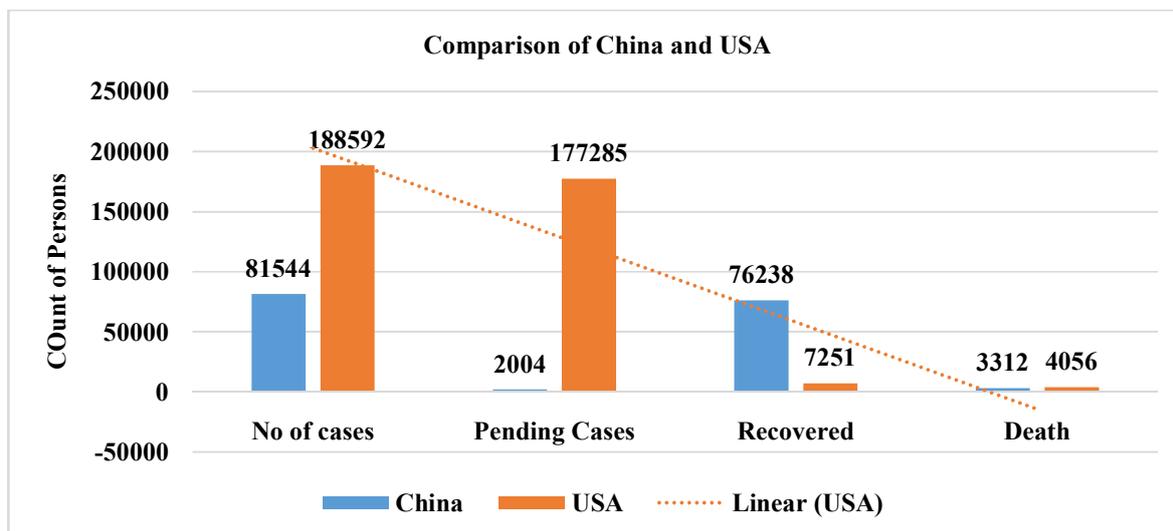


Figure 3: Comparison of China and USA

Table 2: Spread across the Africa

S/no	Countries of Africa	No of Cases
1	Algeria	454
2	Egypt	576
3	Libya	3
4	Morocco	450
5	Tunisia	278
6	Benin	6
7	Burkina Faso	222
8	Cape Verde	5
9	The Gambia	3
10	Ghana	152
11	Guinea	8
12	Guinea-Bissau	2
13	Ivory Coast	165
14	Liberia	3

.	Mauritania	5
16	Mali	18
17	Nigeria	111
18	Niger	20
19	Senegal	142
20	Togo	30
21	Cameroon	113
22	Central African Republic	6
23	Chad	5
24	Congo-Brazzaville	19
25	DR Congo	65
26	Equatorial Guinea	13
27	Gabon	7
28	Angola	3
29	Eswatini	9
30	Madagascar	44
31	Mozambique	8
32	Namibia	6
33	South Africa	1250
34	Zambia	29
35	Zimbabwe	7
36	Djibouti	15
37	Eritrea	12
38	Ethiopia	21
39	Kenya	38
40	Mauritius	102
41	Rwanda	60
42	Seychelles	8
43	Somalia	3
44	Sudan	5
45	Tanzania	13
46	Uganda	33
	TOTAL	4613

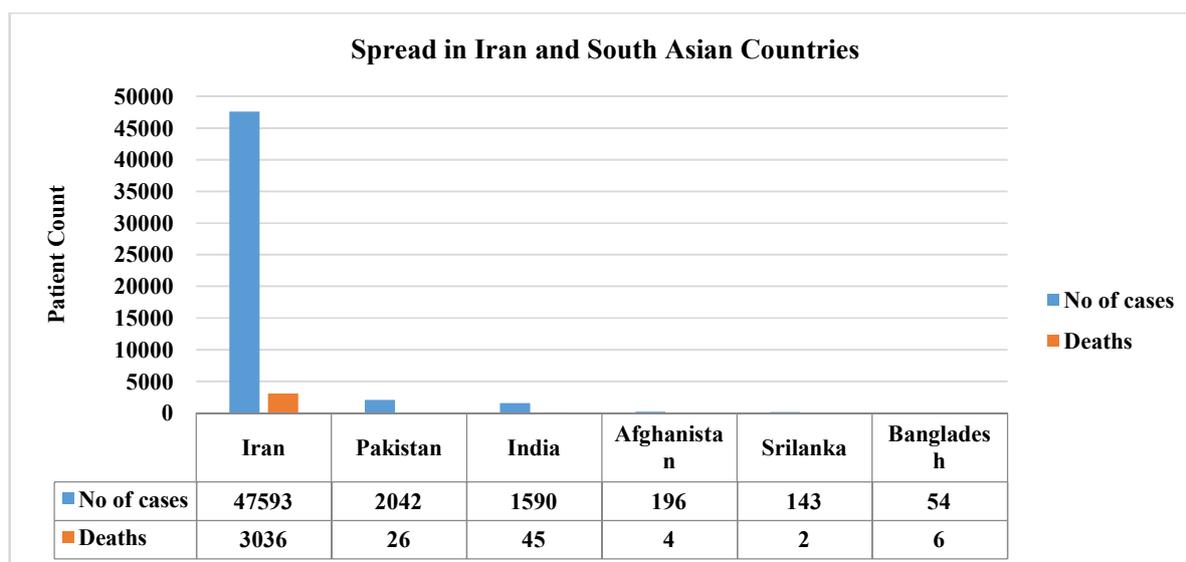


Figure 4: Spread in Iran and South Asian Countries

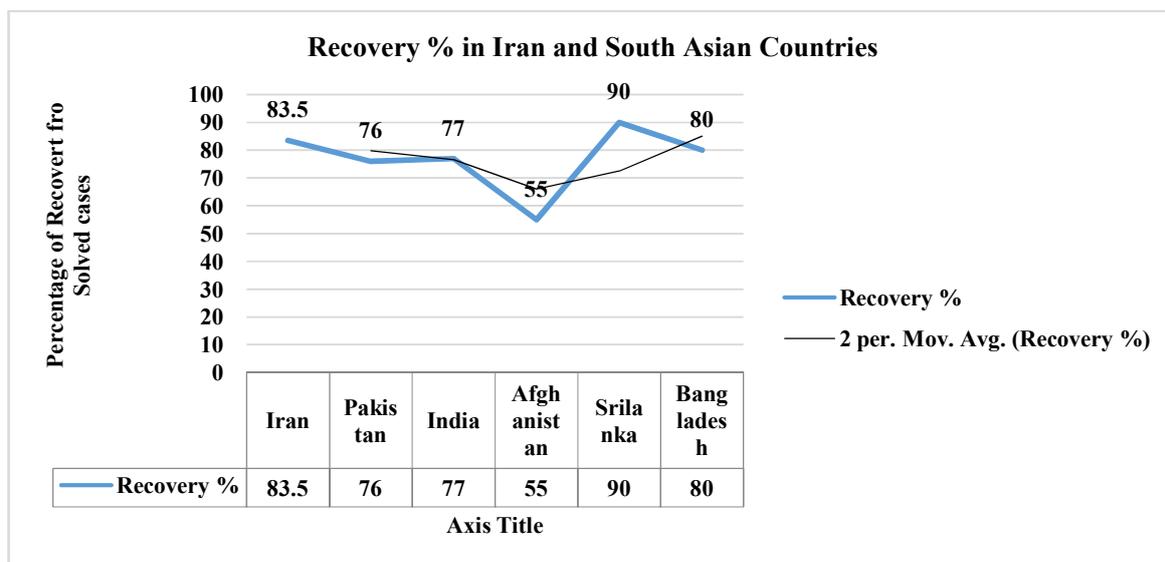


Figure 5: Recovery % in Iran and South Asian Countries

Table 3: Spread across the US states

S/no	States of US	No of Cases	No of Deaths	Population 2020 census	Percent Population Affected
1	New York	75,983	1,714	19,440,469	0.39085
2	New Jersey	18,696	267	8,936,574	0.209208
3	California	8,588	183	39937489	0.021504
4	Michigan	7,615	259	10,045,029	0.075809
5	Florida	6,741	85	21,992,985	0.030651
6	Massachusetts	6,620	89	6,976,597	0.094889
7	Illinois	5,994	99	12,659,682	0.047347
8	Washington	5,482	225	7,797,095	0.070308
9	Louisiana	5,237	239	4,645,184	0.11274
10	Pennsylvania	4,961	63	12,820,878	0.038695
11	Georgia	4,117	125	10,736,059	0.038347
12	Texas	3,715	56	29,472,295	0.012605
13	Connecticut	3,128	69	3,563,077	0.087789
14	Colorado	2,966	69	5,845,526	0.05074
15	Indiana	2,565	65	6,745,354	0.038026
16	Tennessee	2,389	23	6,897,576	0.034635
17	Ohio	2,199	55	11,747,694	0.018719
18	Maryland	1,985	31	6,083,116	0.032631
19	North Carolina	1,536	10	10,611,862	0.014474
20	Virginia	1,484	34	8,626,207	0.017203
21	Wisconsin	1,351	25	5,851,754	0.023087
22	Missouri	1,327	14	6,169,270	0.02151
23	Arizona	1,289	24	7,378,494	0.01747
24	Nevada	1,113	18	3,139,658	0.03545
25	South Carolina	1,083	22	5,210,095	0.020787
26	Alabama	993	23	4,908,621	0.02023
27	Mississippi	937	20	2,989,260	0.031346
28	Utah	887	5	3,282,115	0.027025
29	Oregon	690	18	4,301,089	0.016042
30	Minnesota	629	12	5,700,671	0.011034
31	Kentucky	591	17	4,499,692	0.013134

32	Oklahoma	565	23	3,954,821	0.014286
33	Idaho	525	9	1,826,156	0.028749
34	Arkansas	523	8	3,038,999	0.01721
35	Iowa	497	7	3,179,849	0.01563
36	District Of Columbia	495	9	720,687	0.068684
37	Rhode Island	488	8	1,056,161	0.046205
38	Kansas	428	9	2,910,357	0.014706
39	New Hampshire	367	3	1,371,246	0.026764
40	Delaware	319	10	982,895	0.032455
41	New Mexico	315	5	2,096,640	0.015024
42	Maine	303	5	1,345,790	0.022515
43	Vermont	293	13	628,061	0.046652
44	Hawaii	224	1	1,412,687	0.015856
45	Montana	208	5	1,086,759	0.019139
46	Nebraska	177	3	1,952,570	0.009065
47	West Virginia	162	1	1,778,070	0.009111
48	Alaska	133	3	734,002	0.01812
49	North Dakota	122	3	761,723	0.016016
50	Wyoming	120		567,025	0.021163
51	South Dakota	108	1	903,027	0.01196
52	Puerto Rico	286	11	3,032,165	0.009432

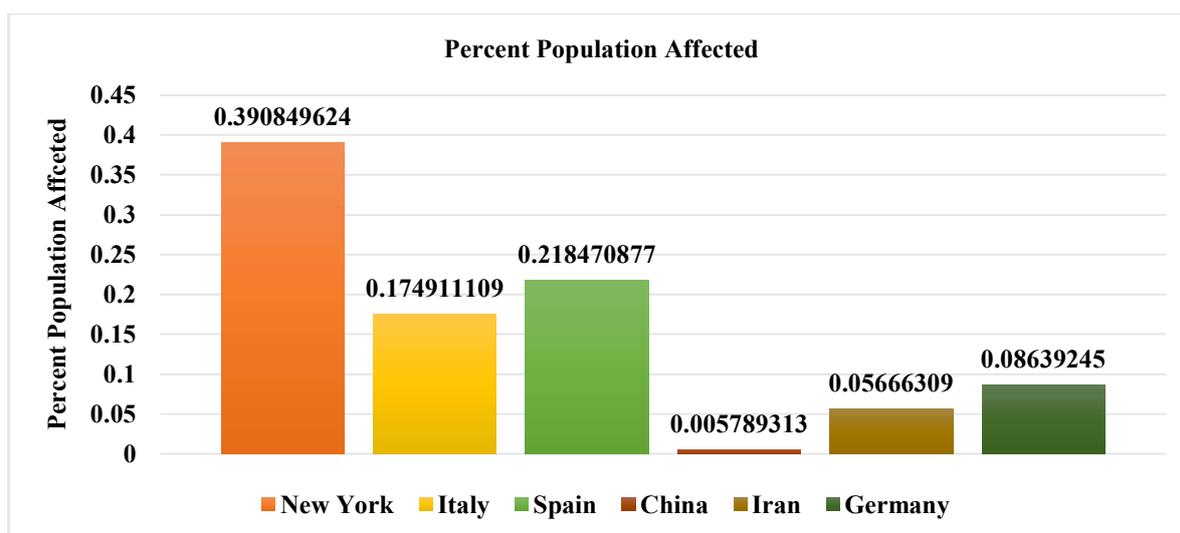


Figure 6: Percent Population Affected

4. MANAGEMENT OF COVID-19

Till date there was no specific treatment for COVID-19 and no vaccine has been formulated despite of fabricated claims from certain parts of world, management is symptomatic. Among various recommendations, we report specific strategies to counter respiratory failure including

mechanical ventilation and high flow nasal oxygen (non-Invasive).

4.1. Mechanical ventilation

Mechanical ventilation with lower tidal volumes (4 to 6 ml/kg predicted body weight, PBW) and lower inspiratory pressures should be used, attainment a plateau pressure (Pplat) < 28 to 30 cm H₂O. PEEP essential be as

high as possible to keep the driving pressure (P_{plat}-PEEP) as low as possible (< 14 cmH₂O). Furthermore, cessations from the ventilator must be ducked for avoiding loss of PEEP and atelectasis. Lastly, the practice of paralytics is not suggested except PaO₂/FiO₂ < 150 mmHg. The prone ventilation for > 12 hours per day, and the use of a conservative fluid administration strategy for ARDS patients.

4.2. Non Invasive

Concerning HFNO or non-invasive ventilation (NIV), the experts suggested that these approaches performed by systems with good interface fitting do not create widespread dispersion of exhaled air, and their use can be considered at low risk of airborne transmission. Practically, non-invasive techniques can be used in non-severe forms of respiratory failure only [20].

4.3. Therapeutic agent

Steroids cannot be prescribed in the infection caused by corona virus. Similarly unsuitable running of antibiotics should be avoided, although some centers recommend it only when patients is admitted in hospital to avoid hospital acquired infection. Till date no antiviral treatments have been approved, several approaches have been proposed such as lopinavir/ritonavir (400/100 mg every 12 hours), chloroquine (500 mg every 12 hours),

and hydroxychloroquine (200 mg every 12 hours). Alpha-interferon (e.g., 5 million units by aerosol inhalation twice per day) is also used. Preclinical studies suggested that remdesivir (GS5734) — an inhibitor of RNA polymerase with in vitro activity against multiple RNA viruses, including Ebola — could be effective for both prophylaxis and therapy of HCoV infections [21]. This drug was positively tested in a rhesus macaque model of MERS-CoV infection. In Italy, a great investigation is focused on the use of tolicizumab. It is a humanized IgG1 monoclonal antibody, directed against the IL-6 receptor and commonly used in the treatment of rheumatoid arthritis [22].

4.4. Chloroquine for management of COVID-19

Chloroquine act as a prophylactic drug and is acting as a therapeutic agent against COVID-19 infection by hitting the virus by three different ways 1st, is Chloroquine acts on host target respiratory cells by increasing the endosomal pH, which dislocate the normal viral function. 2nd In SARS-coronavirus, which is associated to COVID-19, chloroquine interfere with the glycosylation of cellular receptors of the virus leading to no connection between host and invader, 3rd proposal is that chloroquine behave as ionophoric agent for zinc ion and

thus increases the flood of zinc ions in to cytosol of host cell, [23] All mentioned proposals restrict COVID-19 to mutate and produce resistance. Initial two pathways help to inhibit the virus to invade on host cell. Person taking chloroquine and not exposed to the COVID-19, and then after virus enter to infect the host cell first two pathways prevent union of virus and host, but if still virus got arrive unluckily, the force of zinc ions stop polymerization of the virus by stop the RNA polymerase and multiplication may inhibited inside the respiratory cell and infection may halt, Zinc is present in sufficient amount in body but not in free state. The increased level of Zinc are non-toxic as it can easily be excreted, Zinc is present in red meat, legumes nuts and milk products, garlic increase the absorption and bio availability of zinc so it is also essential to use on daily basis[24, 25].

4.5. The Front line immune response

To ascertain the aftermath of an infection the viral interactions with the host immune system plays a significant role. However during initial stages of infection, proteins and Type I interferons (IFN). The innate response of the host at early phases plays a vital role in bringing the adaptive immune response, conversely it has also be seen that at times this intensive immune response may

also cause immune pathology ensuing tissue damage [26]. However few studies also shows that numerous viruses have specific genes which codes for the products that may estrange innate and acquired immune response [26, 27].

Macrophages and dendritic cells are the exclusive components of the innate immune response. Against viral pathogens the dendritic cells which are convened into myeloid dendritic cells (mDC) and plasma cytotoid dendritic cells (pDC) play vital role in steering innate and adaptive immune response [28, 29].

Enormous amounts of type I IFN are rapidly produce when pDCs respond to the viruses .These IFNs prompt the production of antiviral responses, moreover it also modulate natural killer cells and CD8 T cells. Many previous studies shows the pathogenesis of SARS CoV brought illness, serum of infected individuals revealed that cytokines were upregulated all through infection [26].

It has been evident from past studies that in serum of infected individuals the levels of IL-6 was upregulated whereas IL-8 and TGF-beta showed decreased levels. While patients who were recovering also showed increase levels of IL-4, IL-10 and IFN γ [30].

In SARS CoV viral spikes contains a specific protein, S protein which mediates a neutralizing antibody response which is entirely protective in the host. However the memory B cell response and these neutralizing antibody titer were found short lived in convalescent SARS CoV patients. Additionally severe reduction of T cells was also analyzed in the serum of infected individuals. However in various follow up studies it has been revealed that in recovered patients specific antibody response against SARS CoV is short lived, the levels of IgA and IgM response persisted for less than six months. Whereas SARS CoV specific IgG displays presence for four months then declined after a year. Regardless of lack of CoV specific memory B cell response, the virus specific memory T cell lasts for up to six years post infection as observed in recovered individual. Similar results were also seen in animal studies that robust response of virus specific T cell was required for protection against SARS CoV. Efforts are needed to consider approaches to boost T cell response for provision of long term memory [31].

5. PREVENTION

Protective actions is the major key to control its spread rather than treatment which is not established so far. As widespread will

increase as long as R_0 is bigger as 1 (COVID-19 is 2.2), controller methods needed on reducing the rate to less than 1 [32].

Segregation of patients and careful infection control is the main feature for prevention, for occasion, droplet, contact, and airborne precautions should be adopted to control the spread. The WHO and other organizations have issued the following general recommendations including, avoid nearby contact with person suffering from acute respiratory infections. Washing of hands frequently, avoidance of insecure contact with animals, Person shaving symptoms of acute airway infection should keep at distance, cover coughs or sneezes with disposable tissues or clothes and wash their hands, strengthen, in particular, in emergency medicine departments, the application of strict hygiene measures for the prevention and control of infections. Individuals that are immunocompromised should avoid public gatherings. Special precautions for healthcare workers is to utilize precautions to include PPE such as N95 or FFP3 masks, eye protection, gowns, and gloves to avoid spread of the invader.

5.1. Prevention Success story of South Korea (Trace, Test and Treat)

The first case in South Korea was reported on 19th February 2020, on 3rd match more than 850 cases were reported and total count was reached to 5186, at that time it was assumed that South Korea will going to face spike like Italy and Spain but at the end of March there were only 9786 cases with 168 death (**Figure 7**) unlike Italy having 105792 cases & 12428 deaths and Spain having 102136 cases and 9053 deaths. South Korea is a populated country having a total count of 51.25 million while Italy and Spain having 60.48 million and 46.66 million respectively. We reported 0.01 % spread (**Figure 8**) in S.

Korea which was extraordinarily less than Italy and Spain.

In 2015 S. Korea faced MERS Virus from that about 36 people were died, keeping this in view CDC of Korea established Department to keep Korea safe from upcoming pandemic disasters. With onset COVID-19, they start corona testing daily for at least 20000 person, 96 specific laboratories were established, 100000 per day emergency testing kit for corona were designed, and then they start to perform 140000 daily test, after completion of their requirement they contact 17.

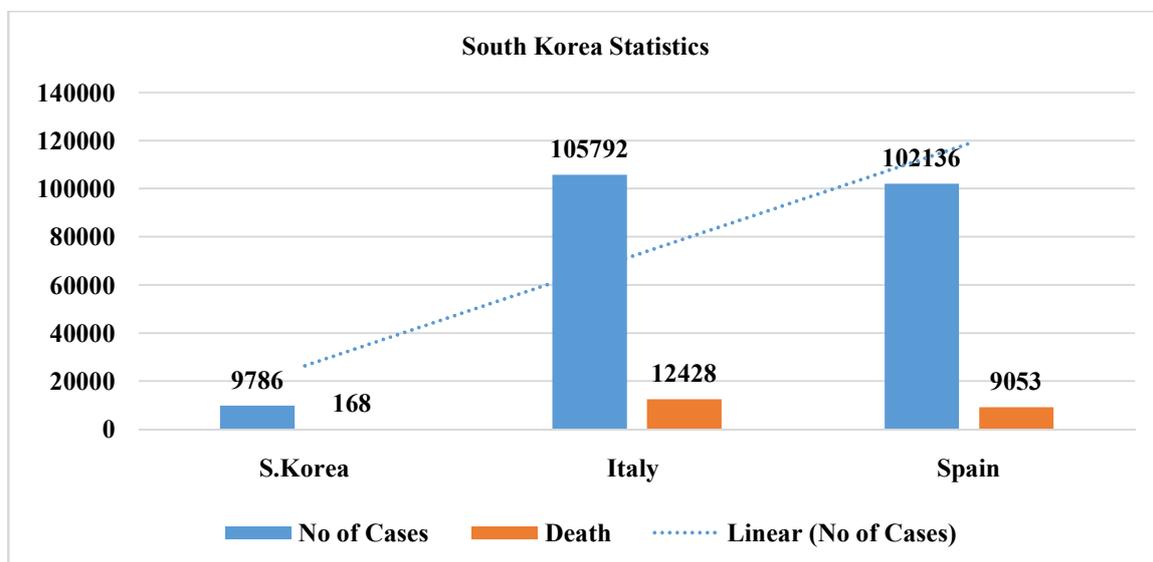


Figure 7: South Korea Statistics

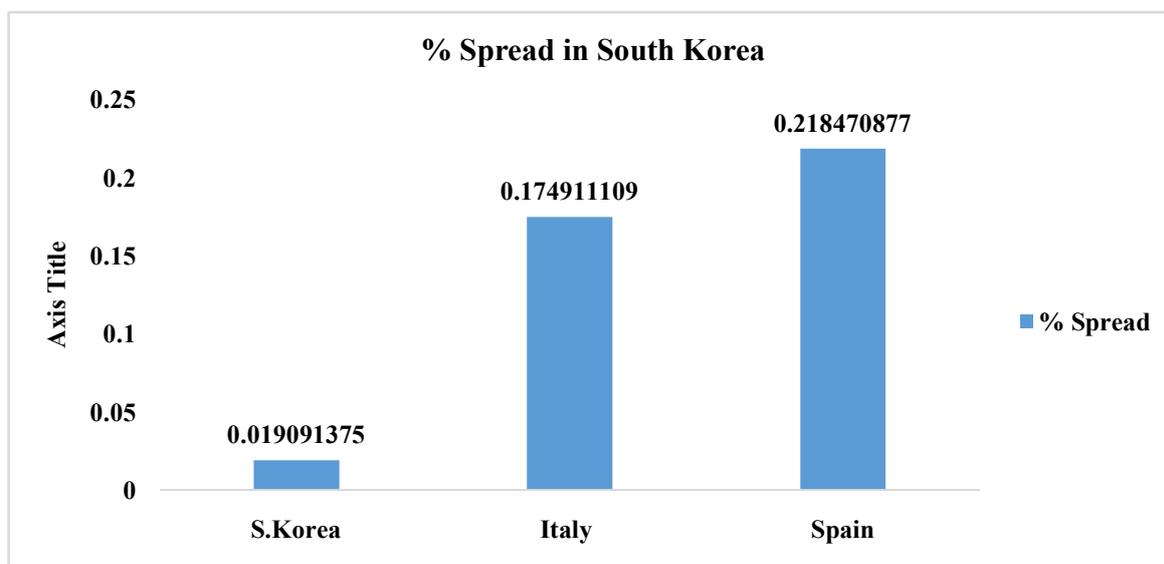


Figure 8: % Spread in South Korea

Other countries to help them out, the accuracy of their testing kit was 98% which is more than 40% from US. To avoid people gathering in hospitals they establish 633 testing centers, sample from people were taken on roads and also from people without getting them off from their cars. The movement of corona carrier person was recorded using CCTV cameras, the use of credit card and GPS, the nearby resident people get alerts on their cellular devices about movement of suspected person even his entry and exit bus station. People were warned on mobile apps and websites about nearby suspected person. The person having corona then quarantined at their own homes and 2500\$ fine was imposed if that person tend to get out from quarantine using GPS

service. They also imposed heavy fine on concerned for increasing price on medical supply. The strategy they used was “Trace Test and Treat”, and they get only 1% of death rate which is 3.4% across the world as per WHO.

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